

# Another Anniversary for the War on Cancer

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**I**n 1993, 526,000 Americans died of cancer—about 1400 people a day—even though conquering cancer became a national goal in December, 1971, now more than 22 years ago. Though tens of thousands of skilled scientists have been waging war against cancer in their laboratories for a generation, spending billions of tax, charitable, and investor dollars, the dread disease remains a metaphor for anything evil in society that spreads. The human statistics should be an issue of the most profound concern to the cancer industry because they are the only true measure of its performance, and the statistics remain very grim.

Why don't we have a cancer cure by now? The answer, in my opinion, is basic and essentially simple: The cell lines in which cancer is usually studied are unsuitable for the job. They do not mimic conditions in the human body.

The cancer industry has ignored the limitations of its most important piece of material—its favorite model—because "Nobody likes to ask if a model is really correct..." (Francis Crick, *What Mad Pursuit*, 1988, Basic Books, New York, p. 161). More than 40 years ago, these long-term cell cultures began their careers as stand-ins for real cancer based only on investigator faith in their reliability. Because they are so convenient for experimentation and the methods of molecular biology, cell lines today have become the standard for determining what cancer should be like. The facts indicate, however, that petri dish cancer is really a poor representation of malignancy, with characteristics profoundly different from the human disease.

When a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary-type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells *in vivo* are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years, evidence that has been systematically ignored by the cancer establishment.

Studies of human and animal cancer have shown that only differentiating, aging cells in organs are susceptible to cancer. Data from undifferentiated, ageless "normal" cell lines—like 3T3 in which the pathways that are struck by cancer, those of develop-

ment and aging, are absent—cannot be relevant to cancer initiation in humans.

The widely disparate character of human tumor cell lines contributes greatly to chemotherapy's continued ineffectiveness against cancer. New drugs are selected for human trials because they kill tumor cell lines in the laboratory.

Surgical pathologists, the specialists who diagnose cancer, have long recognized that cancer cells are just misbehaving body cells. In other words, the immune system registers self when confronted by a malignant cell. This means that several decades of highly publicized, well-funded research on immunotherapy has produced only mice that are cured of their cell line tumors.

The standard approach of most cancer scientists to experimentation produces little of practical value because it is flawed. Typically, an observation is first made in culture, then the investigator turns to human cancer. If the observation is duplicated, papers are written about the significant find. But, if you look long and hard enough *in vivo* you will always find what you seek. For example, there may be a rare human tumor that is immunogenic, but this is just the exception that proves the rule. There are human tumors in which a proto-oncogene is mutated, but there are others of the same type in which it is not. What is significant in culture, for example immunotherapy's killing power or the transformation of 3T3 cells by a mutated proto-oncogene, simply does not have the same significance for cells *in vivo*. Instead of this approach, models that mimic the human body and the developmental pathways of human cells, both normal and malignant, should be first identified. Only then will truly significant observations be made.

How cancer is defined today depends on what courses have been taken, what books have been read, which journals have been studied, and what research training and practice have been followed. The result is confusion. An unnatural condition created in the laboratory is being mistaken for human cancer.

Every year, for as long as I can remember, cancer scientists and cancer physicians have met during the same week, under one roof, at overlapping conferences. They no longer will do so. This year, the American Association for Cancer Research and the American Association of Clinical Oncology begin meeting separately. The new meeting policy, initiated by the researchers, is as open an admission as one is likely to get from them that they really haven't been interested in the real world for a long time. ///